

# Global Prevalence of Anemia Among Type 2 Diabetic Adult Patients: A Systematic Review and Meta-Analysis

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**Background:** Anemia is a common and often overlooked hematological change observed in patients with diabetes mellitus. However, there is no global survey or health registry that estimates the pooled prevalence of anemia in patients with type 2 diabetes. Therefore, this study aimed to determine the global pooled prevalence of anemia among adult patients with type 2 diabetes.

**Methods:** This study was conducted in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analysis guidelines. The study protocol was registered on PROSPERO with the reference number (CRD42022327135), and the link provided ([https://www.crd.york.ac.uk/prospero/display\\_record.php?ID=CRD42022327135](https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022327135)) display the published methodology. Previously published articles were searched in PubMed/Medline, Cochrane Library, WHO Global Index Medicus, African Journals Online, ScienceDirect, Google Scholar, and Google from October 26 to November 09, 2022. The quality of the included studies was assessed using the Joanna Briggs Institute Critical Appraisal tool. Random-effects model was used to estimate the pooled prevalence of anemia. The degree of heterogeneity among the included studies was assessed using  $I^2$  statistics. Publication bias was detected using funnel plot symmetry analysis supplemented by Egger's and Begg's tests.

**Results:** Twenty-four studies with a total number of 19,118 participants were included in this systematic review and meta-analysis. The overall pooled prevalence of anemia among type 2 diabetic adult patients was 27.0% (95% CI: 24.0, 31.0,  $I^2 = 96.45\%$ ;  $P < 0.001$ ). Geographical and time-based subgroup analysis showed that higher prevalence of anemia was observed in Africa region 28.0% (95% CI: 17.0, 39.0) and from 2015 to 2022, 28.0% (95% CI: 24.0, 33.0), respectively.

**Conclusion:** Anemia is a moderate public health problem among adult patients with type 2 diabetes. Nearly one in four patients with type 2 diabetes develops anemia. Therefore, considering the negative impact of anemia, it is important to include anemia screening in the routine assessment of diabetes-related complications.

**Keywords:** adult, anemia, inflammation, type 2 diabetes, meta-analysis, systematic review

## Introduction

Diabetes is a fast-growing global health emergency characterized by persistent hyperglycemia, with changes in the metabolism of carbohydrates, lipids, and proteins resulting from defects in insulin secretion, action, or both.<sup>1</sup> The burden of diabetes among adults has rapidly increased, from 108 million in 1980 to 537 million cases and 6.7 million deaths by 2021.<sup>2</sup> More than two-thirds of the global burden of diabetes is observed in low- and middle-income countries, and the number of diabetes cases is estimated to increase to 783 million by 2045.<sup>2</sup> Uncontrolled diabetes is associated with various pathological changes, including metabolic, cellular, and blood disturbances, resulting in long-term microvascular and macrovascular complications.<sup>3</sup>

Type 2 diabetes mellitus (T2DM) accounts for 90–95% of diabetes cases<sup>1</sup> and it is a part of metabolic syndrome that comprises dyslipidemia, obesity, hypertension, and hematological changes.<sup>4</sup> Hematological changes, including those in red blood cells (RBCs), white blood cells (WBCs), platelets, and coagulation systems, have been documented in diabetes.<sup>5</sup> Anemia is the most common and often overlooked hematological change observed in patients with

T2DM.<sup>6,7</sup> The etiology of anemia in T2DM is multifaceted and includes impaired renal function, hormonal changes, oral hypoglycemic agents, oxidative stress, advanced glycation end-products (AGEs), chronic hyperglycemia, and inflammation.<sup>8–12</sup> Advanced aged subjects with anemia usually tend to have chronic comorbidities including diabetes mellitus.<sup>13</sup> In addition, type 2 diabetes mellitus is associated with increased burden of chronic low-grade inflammation which can drive bone marrow and other mechanism to produce anemia.<sup>14</sup> Regardless of the underlying mechanisms of diabetogenesis, anemia is an independent predictor of increased risk of vascular complications in diabetes.<sup>15,16</sup> Early diagnosis and treatment of anemia in diabetes have been shown to improve complications,<sup>15,17</sup> as it occurs early in the progression of diabetic nephropathy and other complications.<sup>18,19</sup>

Anemia is amongst the major clinical and public health challenges that influence the progression of chronic health problems in diabetic population.<sup>20</sup> However, the precise prevalence and characterization of anemia in the diabetic cohort is unknown. There is a need of identifying and monitoring of iron status and anemia in patients with T2DM.<sup>21</sup> Recently published systematic review and meta-analysis showed that anemia is a moderate to severe public health problem among adult populations living with diabetes, with the prevalence of 22% in Ethiopia, 35% in Africa, and 45% in South Asia.<sup>20,22,23</sup>

Despite a growing body of research on these problems, there is a lack of synthesized evidence on the burden of anemia among people with diabetes. Although some studies have been conducted on the prevalence of anemia, no official worldwide survey or international health registry has estimated the prevalence of anemia in T2DM patients to date. Therefore, this study aimed to determine the global pooled prevalence of anemia in type 2 diabetic adult patients.

## Methods

### Study Setting, Design and Protocol

This systematic review and meta-analysis were conducted for all cross-sectional studies published worldwide. The Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) 2020 checklist (S1)<sup>24</sup> was used throughout the review process. The study protocol was prospectively registered on PROSPERO (registration number CRD42022327135), and the link provided ([https://www.crd.york.ac.uk/prospero/display\\_record.php?ID=CRD42022327135](https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022327135)) shows the published methodology.

### Searches Strategy

A literature search was conducted from major databases and indexing services including PubMed/Medline, Cochrane Library, WHO Global Index Medicus, African Journals Online, ScienceDirect, Google Scholar, and Google from October 26, to November 09, 2022. Search terms were used either separately or combination with Boolean operators (OR and AND). The search terms included MeSH (“anemia” OR “anaemia”) AND (“type 2 diabetes mellitus” OR “diabetes mellitus”), AND (“adult”), Title/Abstract (“hematological parameters”), (“anemia” AND “type 2 diabetes mellitus”) (S2). In addition, the reference lists of retrieved articles were used to identify studies that were not retrieved from electronic databases.

### Outcomes of the Study

The main outcome of interest was the global prevalence of anemia among adult patients with type 2 diabetes according to the World Health Organization (WHO) definition of anemia (hemoglobin (Hgb) value less than 13 g/dl for men and less than 12 g/dl for non-pregnant women).<sup>25</sup>

### Eligibility Criteria

To make the review more manageable and applicable, studies employing a cross-sectional design were considered. Therefore, all cross-sectional studies available online from January 1, 2000, to November 09, 2022, and the reported prevalence of anemia among adult patients with type 2 diabetes were included in the review. In contrast, studies that reported complications of diabetes but did not report separate outcomes for anemia were excluded. In addition, non-cross-sectional studies (clinical audit, case reports, case series, case control, cohort, and RCT), reviews, meta-analyses, studies with low-quality scores according to the criteria, and studies addressing specific groups such as HIV-infected adults,

tuberculosis, and malaria were not included. Studies that recruited participants with gestational diabetes, type 1 diabetes, or irretrievable studies (after requesting the corresponding authors) were excluded.

## Study Selection and Quality Assessment

ENDNOTE version 20 (Thomson Reuters, Stamford, CT, USA) was used to manage search results and identify duplicate records. The titles and abstracts of the studies retrieved using the search strategy were independently screened by two authors (MA and TT) to identify studies that met the inclusion criteria. Subsequently, studies that met the inclusion criteria by title/abstract screening were independently subjected to full-text appraisal by two authors (MA and TT) for eligibility and data extraction. Discrepancies were infrequent between the two authors' evaluations, and when they occurred, they were resolved by sending them to the other authors (HA and KG) to arrive at a consensus. Quality assessment was performed using Joanna Briggs Institute (JBI) critical appraisal tools for prevalence studies in a systematic review.<sup>26</sup> Two authors (MA and HA) independently assessed the risk of bias in the included studies. Discrepancies between the two authors were resolved via discussion and by sending them to the other authors (TT and KG). The JBI critical appraisal tool contains nine criteria, and for each criterion, a score was assigned as 0 for "not clear or not appropriate" and 1 for "yes". The average scores given by the two authors were summarized across items to obtain a total quality score ranging from 0 to 9. Studies were then classified as low, medium, and high quality when the average awarded scores were 0–4, 5–7, and 7–9, respectively. All studies with high and medium quality were included in this systematic review and meta-analysis (Table 1).

## Data Extraction

A Microsoft Excel spreadsheet was used to extract data from relevant studies. Two review authors (MA and KG) independently extracted data on author name, year of publication, sample size, study design, year of study, sex, mean/median age of study participants, study setting/country, duration of diabetes, and prevalence of anemia (Table 1).

## Data Analysis

All relevant extracted data were exported to Stata/MP version 17 (Stata Corp, College Station, TX, USA) for the analysis. A narrative synthesis of the data was used to present the included studies, and a summary table was prepared to describe characteristics of the included studies. The pooled prevalence of anemia was carried out using a Der-Simonian-Laird random effects model, along with 95% confidence interval. The degree of heterogeneity among the included studies was assessed using  $I^2$  statistics. The 25%, 50%, and 75%  $I^2$  values were considered as low, moderate, and high heterogeneity, respectively.<sup>51</sup> Subgroup analysis and univariate meta-regression models were used to assess the possible sources of heterogeneity. Potential outliers were investigated in the sensitivity analysis by omitting each study at a time. Publication bias was detected using funnel plot symmetry supplemented by Egger's regression and Begg's tests.<sup>52,53</sup>

## Results

### Search Results

The PRISMA 2020 flow diagram<sup>24</sup> was used to identify, screen, and include the relevant studies (Figure 1). In our comprehensive search, 1108 articles were identified from different sources. Of the total articles, 54 duplicate articles were excluded using EndNote 20 and manual tracing. The remaining 1054 articles were screened by reading their titles and abstracts; 992 articles were excluded. Of the 62 studies sought for retrieval, 4 articles were not accessible in full text, and 58 articles were screened for full-text assessment. Finally, 34 articles were excluded for various reasons and 24 articles were included in the synthesis and analysis.

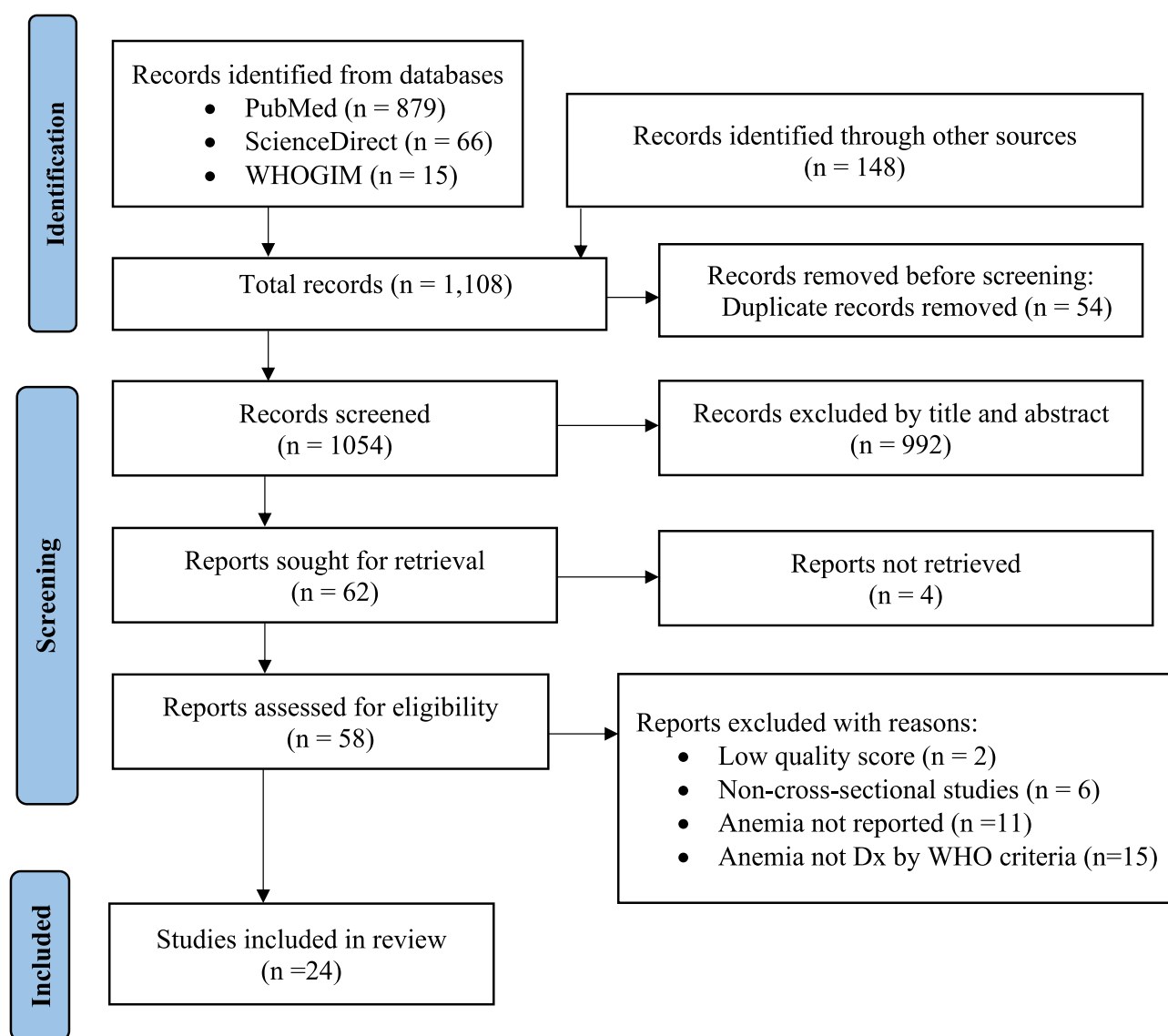
### Characteristics of the Included Studies and Study Participants

Twenty-four cross-sectional studies published between 2006 and 2022 were included in this systematic review and meta-analysis. Fifteen countries were represented and 13 (54.16%) studies were reported in Asia,<sup>28–32,37,38,43–48</sup> followed by

**Table 1** General Characteristics and Outcomes of the Included Studies Among Type 2 Diabetic Adult Patients

Author, Year of Publication	Study Setting	Study Year	Sample Size	Study Design	Sex (M/F)	Mean Age (Years)	DM Duration (Years)	Prevalence of Anemia, n (%)	Quality Score (JBI)
Awofisoye et al, 2019 <sup>27</sup>	Nigeria	2014	155	CS	45/110	60.3 ± 10.2	7 (1–36)	70 (45.1)	8
Chung et al, 2019 <sup>28</sup>	Republic of Korea	2017	1637	CS	797/840	59.8 ± 13.0	NR	579 (35.4)	8
Chung et al, 2017 <sup>29</sup>	Republic of Korea	2014	2230	CS	1083/1147	NR	NR	750 (33.6)	8
Hosseini et al, 2014 <sup>30</sup>	Iran	2011	305	CS	144/161	53.9 ± 1	8.2 ± 7.1	93 (30.4)	7
Praveen et al, 2020 <sup>31</sup>	India	NR	89	CS	NR	49.76 ± 10.3	NR	15 (16.8)	7
Rathore et al, 2018 <sup>32</sup>	India	2016	200	CS	126/74	56.8	5	65 (32.5)	6
Bekele et al, 2019 <sup>33</sup>	Ethiopia	2019	374	CS	176/198	56.3 ± 11.5	5 (1–30)	130 (34.8)	8
Arkew et al, 2021 <sup>34</sup>	Ethiopia	2020	134	CS	85/49	43.08±9.3	7.0 (4.0–9.0)	24 (17.9)	8
Ebrahim et al, 2022 <sup>35</sup>	Ethiopia	2021	120	CS	64/56	38.75 ±10.5	5	31 (25.8)	8
Kebede et al, 2021 <sup>36</sup>	Ethiopia	2019	372	CS	142/230	NR	8.87 ± 3.69	30 (8.0)	8
He et al, 2015 <sup>37</sup>	China	2008	1997	CS	1141/856	59.67 ± 12.2	8.06 ± 6.71	439 (22.0)	7
Wu et al, 2017 <sup>38</sup>	China	NR	1134	CS	645/489	57.1 ± 9.6	9 (4–13)	231 (20.4)	7
Srivastava et al, 2006 <sup>39</sup>	Australia	NR	228	CS	144/84	62 ± 11	10	49 (21.4)	5
Feteh et al, 2016 <sup>40</sup>	Cameroon	2013	636	CS	338/298	56.5 ± 10.6	4 (1–9)	263 (41.3)	6
Ezenwaka et al, 2008 <sup>41</sup>	Caribbean	2006	155	CS	46/109	65.9 ± 0.9	10.6 ± 0.7	72 (46.4)	6
Brière et al, 2020 <sup>42</sup>	France	2019	4145	CS	2226/1919	54 ± 16	15 ± 12	1065 (25.7)	5
Grossman et al 2014 <sup>43</sup>	Israel	2010	445	CS	401/44	63±9.6	6.1±2.9	48 (10.7)	5
Idris et al, 2018 <sup>44</sup>	Malaysia	2015	808	CS	454/354	60.5 ± 9.5	7.0 (8.0)	256 (31.6)	8
Sarosh et al, 2022 <sup>45</sup>	Pakistan	2021	200	CS	82/118	49.64±13	5.98 ± 4.6	78 (39.0)	6
Al-ghazaly et al, 2019 <sup>46</sup>	Yemen	2016	324	CS	141/183	53 ± 12	NR	77 (23.7)	7
Chiou et al, 2015 <sup>47</sup>	Taiwan	NR	1142	CS	579/563	63 ± 11	11 ± 7	286 (25.0)	6
Bonakdaran et al, 2011 <sup>48</sup>	Iran	NR	1962	CS	858/1104	52.47 ± 10.20	7.5 ± 6.1	385 (19.6)	5
Solomon et al, 2022 <sup>49</sup>	Ethiopia	2020	135	CS	NR	44.65 ± 17.69	6.5±5.8	31 (22.9)	8
Abate et al, 2013 <sup>50</sup>	Ethiopia	2012	191	CS	NR	40.96 ± 16.8	5.87 ± 4.7	57 (29.8)	8

**Abbreviations:** CS, cross-sectional; NR, not reported.

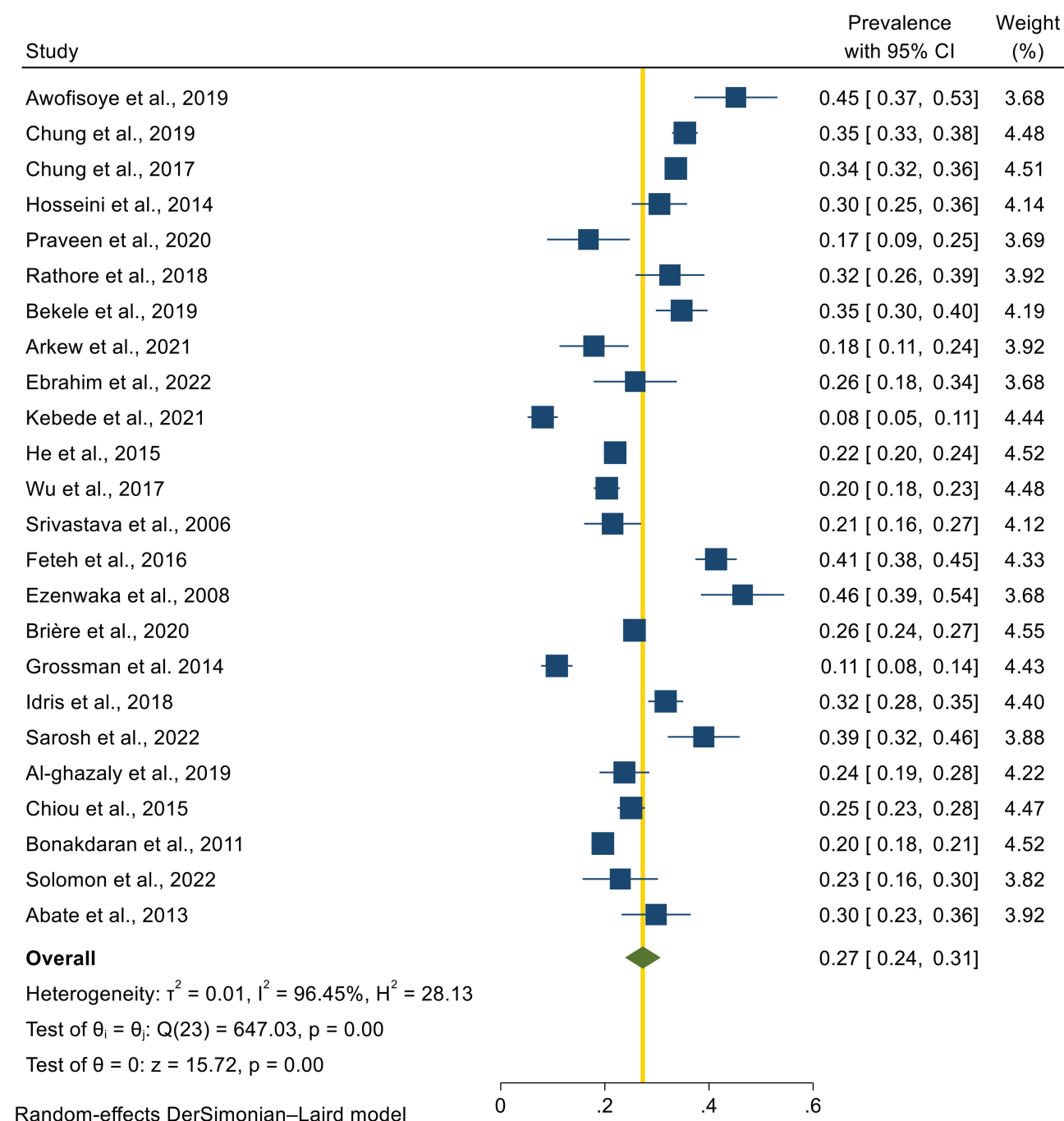


**Figure 1** PRISMA 2020 Flow chart to describe the selection of studies for the systematic review and meta-analysis on the global prevalence of anemia among T2DM adult patients.

eight (33.33%) studies from Africa,<sup>27,33–36,40,49,50</sup> one (4.17%) study from Europe,<sup>42</sup> one (4.17%) study from Australia,<sup>39</sup> and one (4.17%) study from South America.<sup>41</sup> The average quality scores of studies ranged from 5 to 8 as per the Joanna Briggs Institute scoring scale for prevalence studies. The sample sizes of the included studies ranged from 89<sup>31</sup> to 4145<sup>42</sup> with a pooled mean sample size of 797.0 and total number of 19,118 participants. The mean age of the participants was reported in 22 studies and ranges from 38.75 to 65.90 years.<sup>35,41</sup> The mean duration of diabetes was reported in 20 studies, ranging from 4 to 15 years, with a pooled mean duration of 7.6 years (Table 1).

## Prevalence of Anemia

This systematic review and meta-analysis included 24 studies, all of which were used to estimate the pooled prevalence of anemia among adult patients with type 2 diabetes. The Random effects analysis revealed that the overall pooled prevalence of anemia among type 2 diabetic adult patients was 27.0% (95% CI: 24.0, 31.0) with higher heterogeneity ( $I^2 = 96.45\%$ ;  $P < 0.001$ ). The prevalence of anemia in individual studies ranged from 8.0% to 46.0%,<sup>36,41</sup> whereas the individual weight ranged from 3.68% to 4.55%<sup>27,35,41,42</sup> (Figure 2). Based on the extent of heterogeneity in the random effects model, the 95% estimated predictive interval was calculated for this study. The estimated predictive interval for the true prevalence of anemia



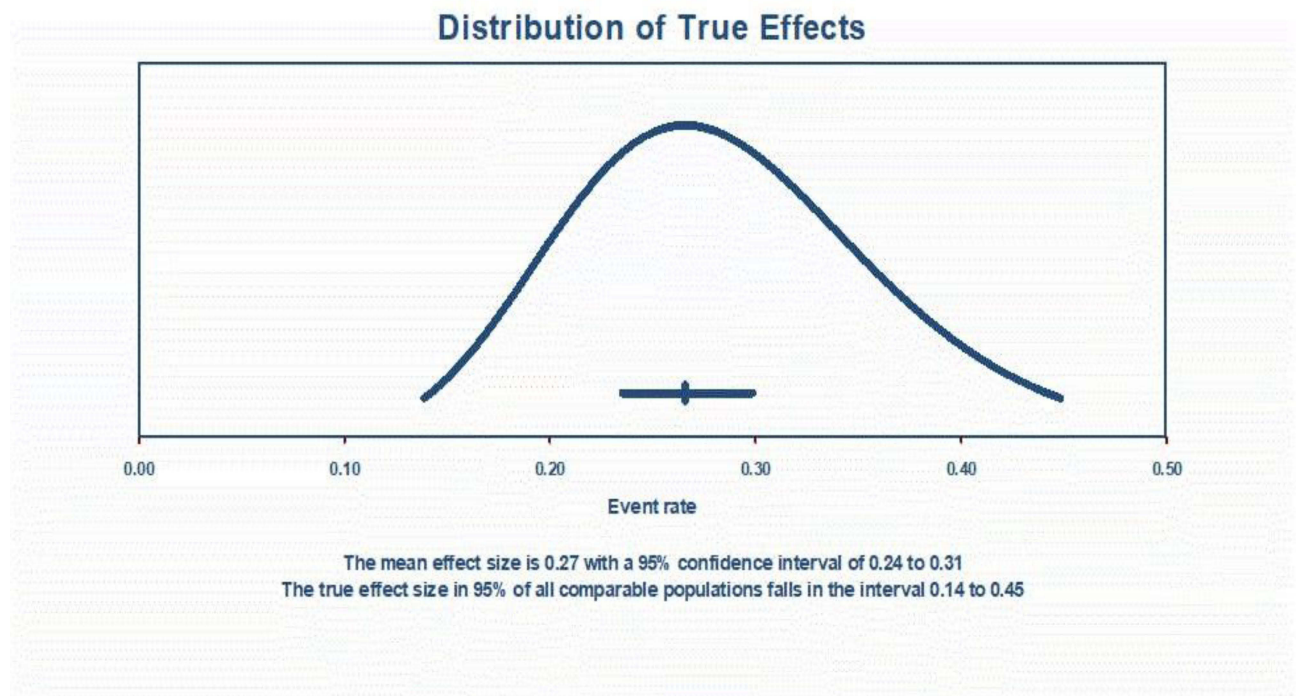
**Figure 2** A forest plot showing the individual study and pooled prevalence of anemia among T2DM adult patients.

is ranged from 14% to 45%, which displays the approximate predictive distribution of any future study for all comparable populations (Figure 3).

## Subgroup and Sensitivity Analysis

To identify the source of heterogeneity across the included studies, subgroup analyses were performed by considering publication year, sample size, duration of diabetes, and geographical region as grouping variables. Time based subgroup analysis showed that the prevalence of anemia from 2015 to 2022 was higher than that from 2006 to 2015 (28.0% vs 25.0%). The results of subgroup analysis based on geographical region showed the highest prevalence was from Africa





**Figure 3** Predictive interval for population prevalence of anemia among T2DM adult patients.

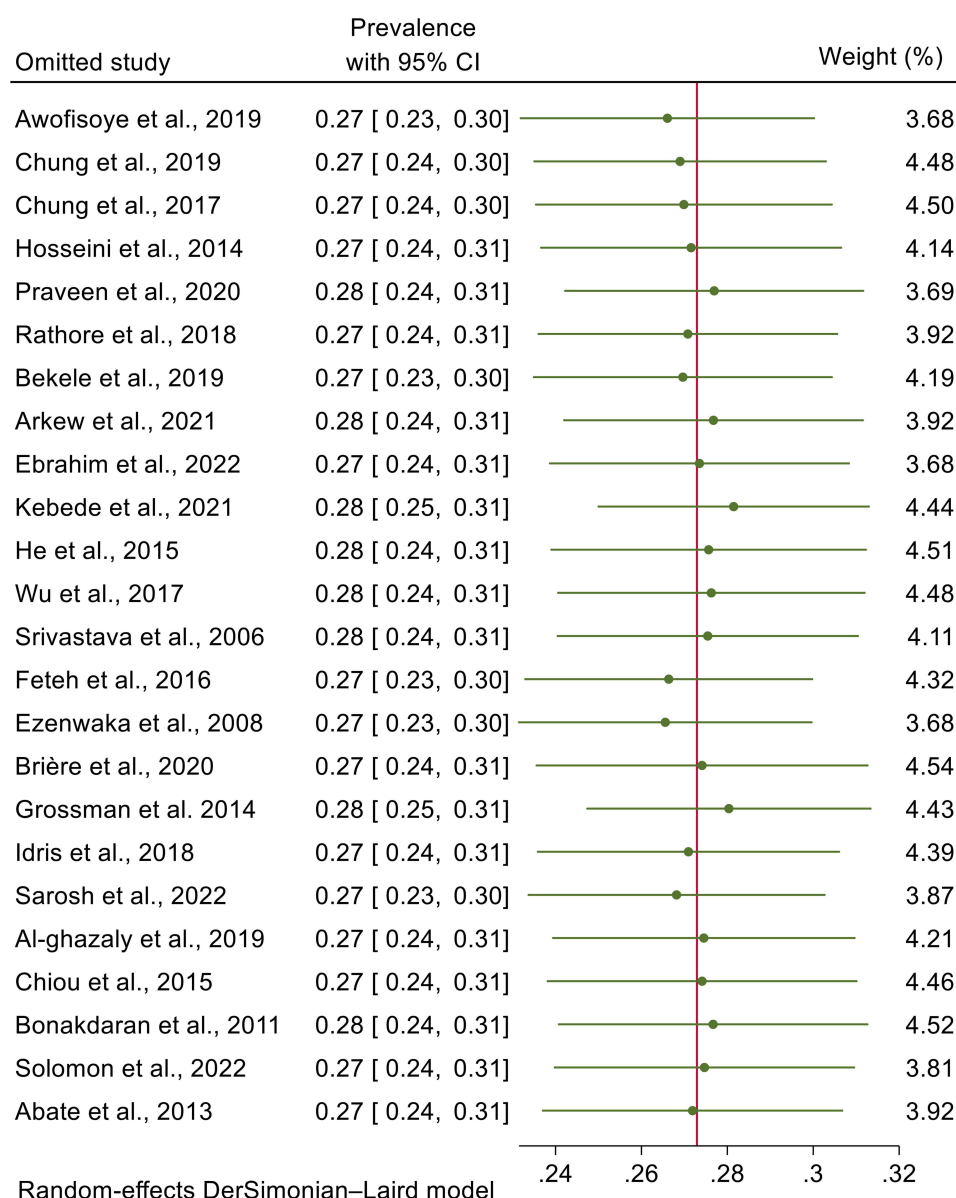
(28.0%) as compared to other regions (Table 2). Additionally, to explore the influence of a single study on the overall meta-analysis, a sensitivity analysis using the leave-one-out approach was conducted. The results revealed that there was no strong evidence for the effect of a single study on the overall meta-analysis result (Figure 4). Furthermore, to investigate the heterogeneity observed in the studies, we performed meta-regression on continuous variables. Accordingly, univariate meta-regression revealed that the mean age of the participants, publication year, sample size, and duration of diabetes were not sources of heterogeneity.

## Publication Bias

Publication bias was assessed visually using a funnel plot and statistically using the Egger's and Begg's tests. The funnel plot (Figure 5) was symmetric, and Egger's regression test ( $P = 0.356$ ) and Begg's test ( $P = 0.385$ ) provided no evidence of publication bias owing to the small study effects.

**Table 2** Subgroup Analyses Showing Pooled Prevalence of Anemia Among Type 2 Diabetic Adult Patients

Subgroups		Number of Studies	Prevalence (95% CI)	Heterogeneity	
				I <sup>2</sup>	P-value
Region	Asia	13	26.0 (22.0, 30.0)	96.61%	<0.001
	Africa	8	28.0 (17.0, 39.0)	97.31%	<0.001
	Europe	1	-	-	-
	Australia	1	-	-	-
	South America	1	-	-	-
Sample size	≤ 797	16	28.0 (21.0, 34.0)	96.29%	<0.001
	> 797	8	27.0 (23.0, 31.0)	96.89%	<0.001
Duration of DM	≤ 7.6	12	29 (23.0, 35.0)	96.14%	<0.001
	>7.6	8	24.0 (20.0, 29.0)	96.08%	<0.001
Publication year	2006–2015	8	25.0 (20.0, 29.0)	94.26%	<0.001
	2015–2022	16	28.0 (24.0, 33.0)	96.53%	<0.001



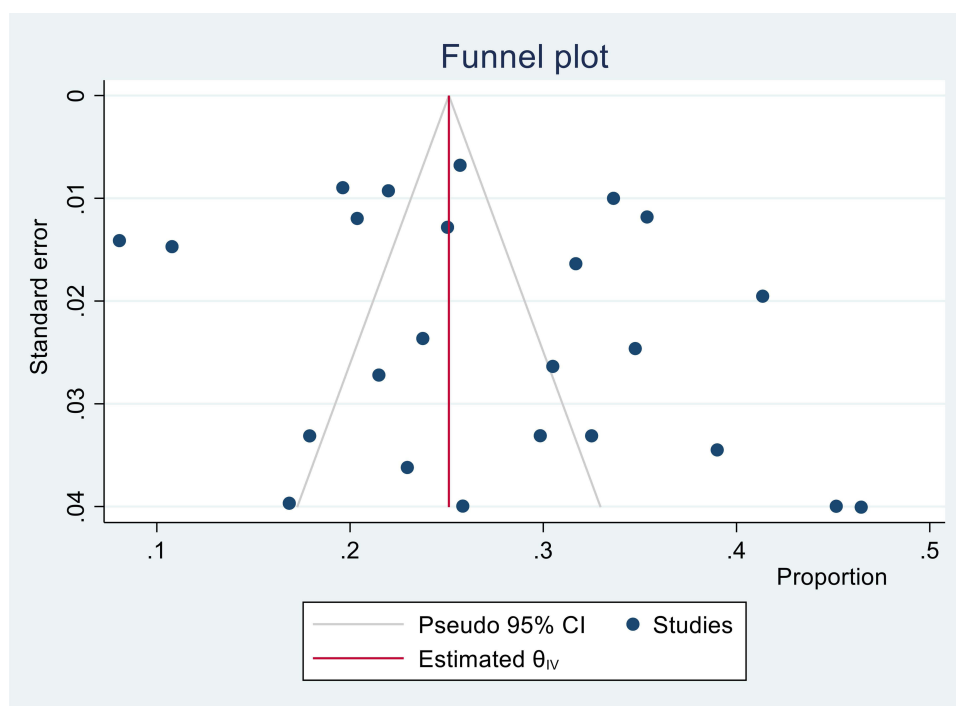
**Figure 4** Sensitivity analysis showing the prevalence of anemia among T2DM adult patients.

## Discussion

Anemia is a major public health problem estimated to affect about 1.74 billion (22.8%) of the world's population and disproportionately affects low and middle-income countries.<sup>54,55</sup> Anemia in individuals with diabetes results in adverse health consequences, as it is associated with the progression of vascular complications and all-cause mortality.<sup>18,19,56</sup> However, a global estimate of the prevalence in type 2 diabetic adult population is lacking. In the current systematic review and meta-analysis, the pooled prevalence of anemia was 27%, which corresponds to moderate public health significance according to the WHO classification.<sup>25</sup> Accordingly, the results of this meta-analysis indicate that anemia is a moderate public health problem among patients with type 2 diabetes, which requires the design of prevention and control strategies to reduce the burden of anemia. This finding is in agreement with those of previous studies,<sup>22,23,57</sup> which reported that anemia is a moderate public health problem in the diabetic population.

In the subgroup analysis, the prevalence of anemia was relatively higher in Africa region as compared to Asia region (28.0% vs 26.0%). This finding is in agreement with the notion that anemia is more prevalent in less developed





**Figure 5** Funnel plot depicting publication bias for the prevalence of anemia among T2DM adult patients.

countries.<sup>55</sup> This might be due to that type 2 diabetic patients are more vulnerable to different forms of short-term and long-term complications, especially in sub-Saharan African countries.<sup>58</sup>

Anemia in T2DM results from various factors including renal function impairment, chronic hyperglycemia, chronic inflammation, oxidative stress, advanced glycation end products, hormonal changes, and oral hypoglycemic agents.<sup>8–12</sup> Diabetes-related chronic kidney disease remains a global public health problem and is associated with high mortality in diabetic patients.<sup>59</sup> Diabetic nephropathy, a common cause of end-stage renal disease, is associated with impaired iron metabolism and reduced erythropoietin production, resulting in the decreased production of red blood cells.<sup>19,60</sup> Autonomic neuropathy is a major complication of uncontrolled diabetes mellitus. As the production and release of erythropoietin are regulated by the autonomic nervous system, a higher incidence of anemia in patients with poorly controlled diabetes might be observed in the absence of renal impairment.<sup>61</sup>

In addition to renal impairment, blood cells remain in a hyperglycemic environment throughout their lifespan are subjected to several structural and functional changes.<sup>62</sup> These changes might be due to the generation of reactive oxygen species and irreversible glycation of hemoglobin and erythrocyte membrane proteins. This leads to decreased deformability, increased aggregation, aging of RBCs, and a reduced lifespan of erythrocytes.<sup>10,63,64</sup> Additionally, oral antidiabetic medications such as metformin<sup>12</sup> and decreased androgen levels<sup>11,65</sup> are associated with the development of anemia in patients with type 2 diabetes mellitus.

Furthermore, while chronic inflammation causes anemia, persistent hyperglycemia in type 2 diabetes is associated with low-grade inflammation and increased levels of proinflammatory cytokines such as interleukin 6 and interleukin-1.<sup>11,66</sup> Thus, inflammation-inducible cytokines and hepcidin play a role in the development of anemia by increasing the retention of iron in reticuloendothelial cells, changing the sensitivity of progenitor cells to erythropoietin, and promoting apoptosis of immature RBCs.<sup>67</sup> Inflammatory markers such as C-reactive protein, neuregulin-4 and hemogram based inflammatory indices are closely associated with type 2 diabetes and its chronic complications including diabetic nephropathy, leading to anemia.<sup>68–70</sup>

To the best of our knowledge, this is the first systematic review and meta-analysis to summarize all the available data on the prevalence of anemia among adult patients with type 2 diabetes. The data generated in this review may provide important insights into the global prevalence of anemia among type 2 diabetes patients, inform public health interventions, and direct future interventional and empirical research. The PRISMA-2020 guidelines were strictly followed

during the review. However, this systematic review and meta-analysis should be interpreted in the light of the following limitations. First, high heterogeneity was observed in both overall and subgroup analysis. Second, only 15 countries were included in this meta-analysis, with over-representation of some regions, such as Africa and Asia, which could skew the data. Third, this study did not explore the potential factors contributing to anemia in patients with diabetes.

## Conclusions

The results of this review show that anemia is a global public health problem in patients with type 2 diabetes. Almost one in four patients with type 2 diabetes develops anemia. Anemia is more common in Africa than in other regions. Therefore, considering the negative impact of anemia, it is important to include anemia screening for routine assessment of diabetes-related complications.

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## Author Contributions

All authors made significant contributions to the work reported in the conception, study design, execution, acquisition, analysis, and interpretation of data. All authors took part in drafting, revising or critically reviewing the article and gave final approval of the version to be published. All authors have agreed to the approval of the final manuscript for publication in the current journal and to be accountable for all aspects of this work.

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## Disclosure

The authors declare that there are no competing interests.

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